

The Evolving Landscape of HIV Diagnosis

Jenny R. McFarlane

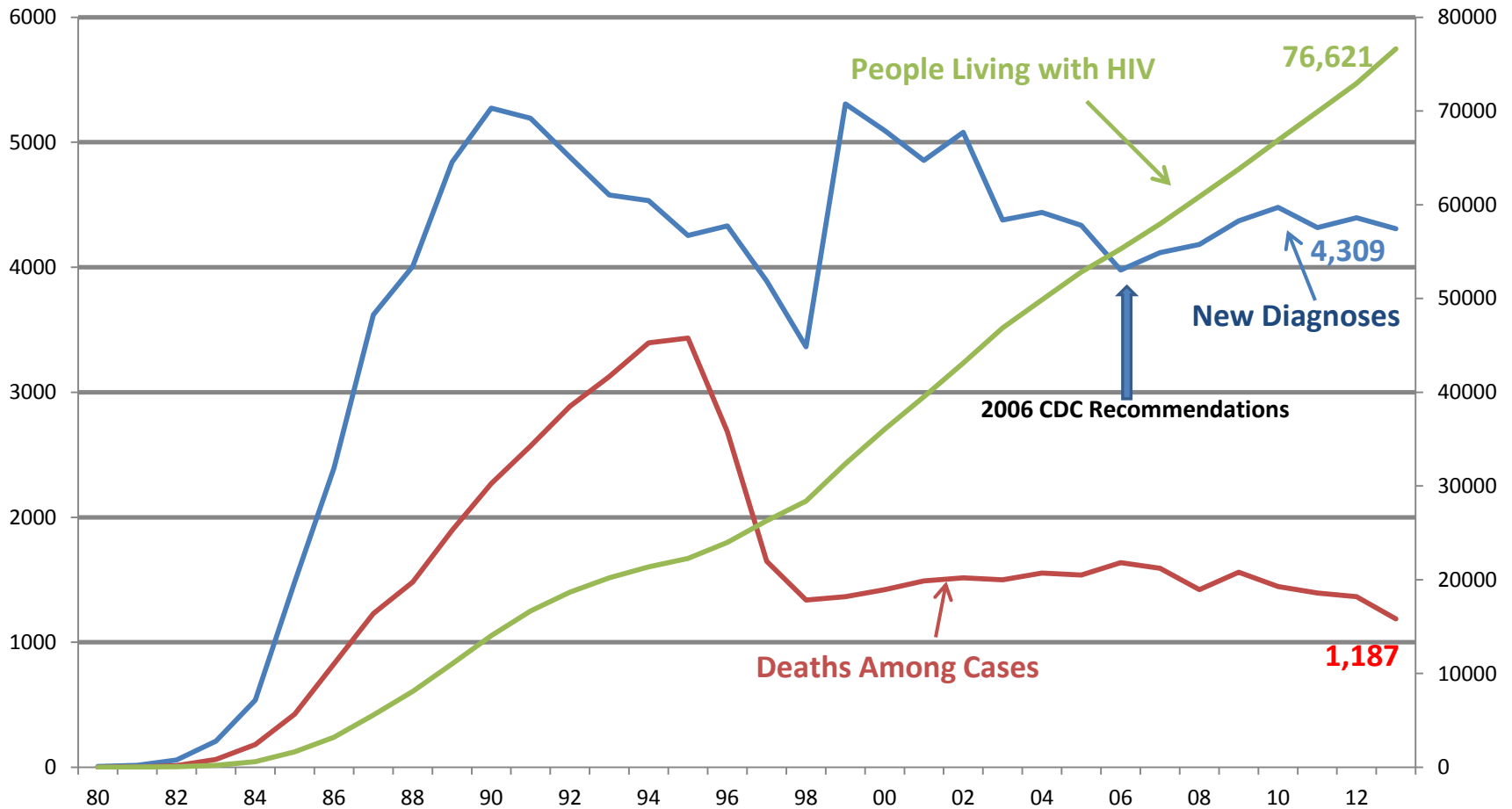
Texas Department of State Health
Services

HIV/STD/TB/Viral Hepatitis Unit

Testing History

- 1985 1st Gen HIV-1 IA
- 1987 HIV-1 WB
- 1990 HIV-2 IA HIV-1 IA DBS
- 1991 2nd Gen HIV 1/2 IA
- 1992 3rd Gen HIV 1/2 IA HIV 1 IFA
- 1994 Oral collection device HIV 1 IA
- 1996 HIV Home Specimen Collection
- Quantitative HIV 1 Viral Load
- 2002 HIV 1 IA Rapid Blood
- 2003 CLIA Waived Rapid IA blood Group O
- 2004 CLIA Waived Rapid HIV 1/2 IA
- Rapid IA Differentiates 1/2
- 2006 Random Access Microparticle CIA
- Qualitative HIV 1 NAT
- 2010 4th Gen Antibody/Antigen
- 2012 CLIA Waived Rapid IA Immediate Results
- Over the counter Rapid IA Oral
- 2013 Rapid 4th Gen Antibody/Antigen

Newly Diagnosed HIV, Deaths, and PLWH, 1980-2013



How far we have come

Cost of a Superbowl ad

- 1989: \$675,000
- 2013: \$3.8 million

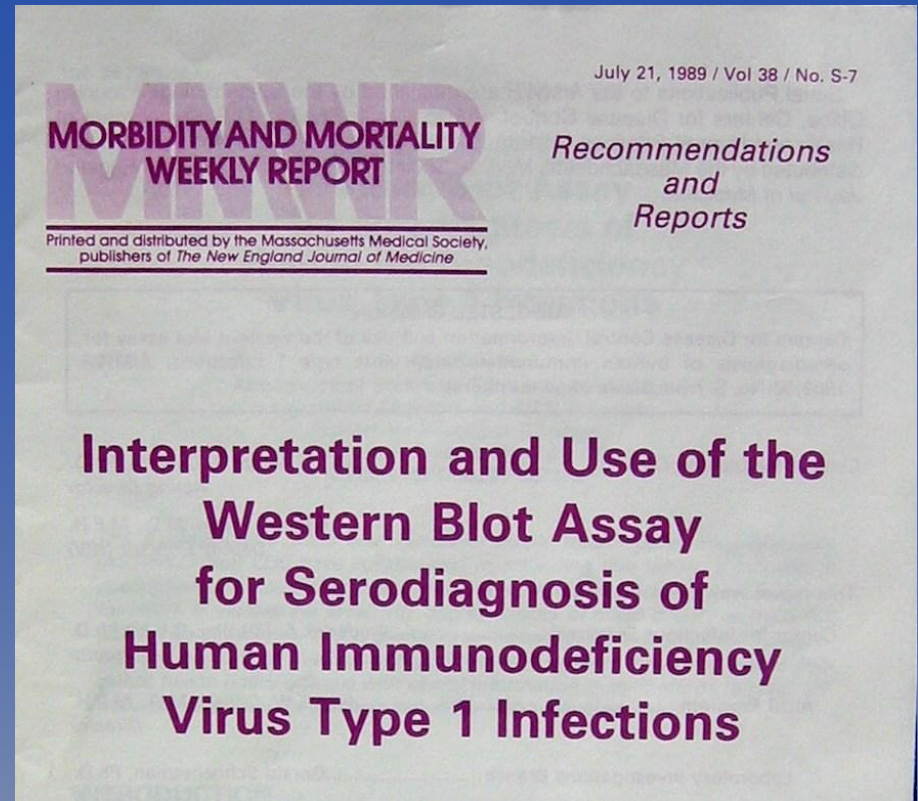
Cell Phones

- 1989 Motorola MicroTAC
\$2500-\$3500
- iPhone, Galaxy, LG, One, Amazon
\$Free with service agreement - \$400



Diagnostic Algorithm since 1989

- The Public Health Service recommends that no positive test results be given to clients/patients until a screening test has been repeatedly reactive on the same specimen and a supplemental, more **specific test such as the Western blot** has been used to validate those results.



Serologic Assay Generations

- 1st generation immunoassays (IA)
 - Detects HIV antibody (Ab) IgG using viral lysates as the antigens (Ag)
- Western BLOT - 1st gen assay





INSTI

2nd Gen CLIA-Waived
Point-of-Care
Rapid HIV Tests
Detects HIV IgG Antibody



Clearview Complete



ChemBio Stat Pak

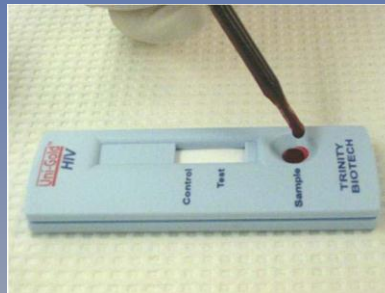


OraQuick Advance

3rd Generation

Detects HIV 1/2 IgG and IgM Antibodies

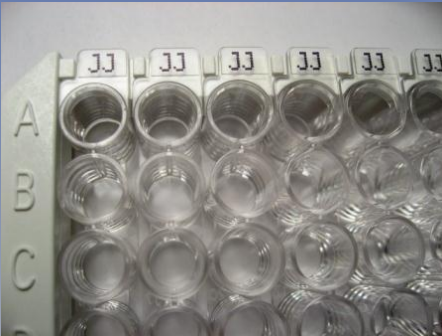
- Unigold
- Siemens ADVIA Centaur - LAB
- Ortho VITROS Sei/ECIQ - LAB
- Ortho GS 1/2 +O - LAB
 - Time to results 48 – 60 minutes



4th Generation

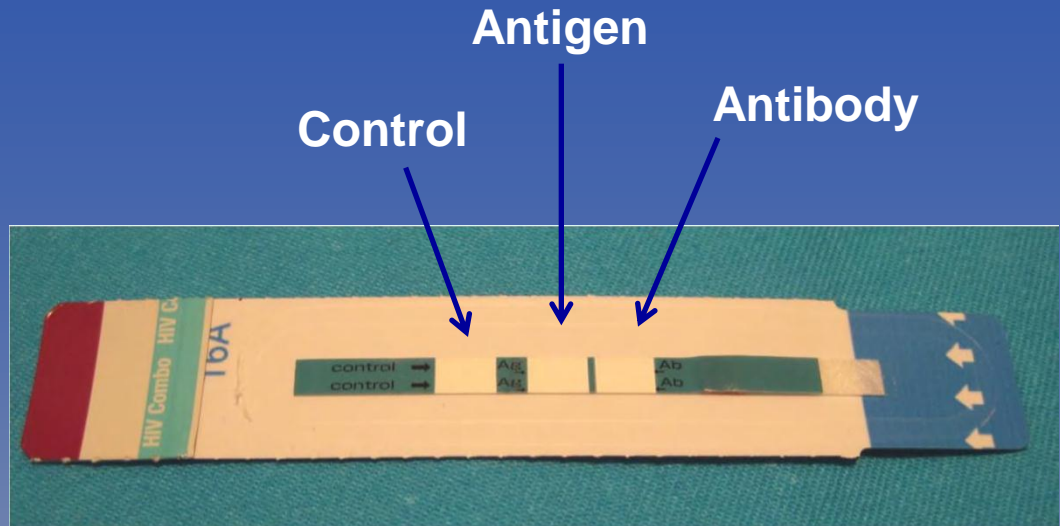
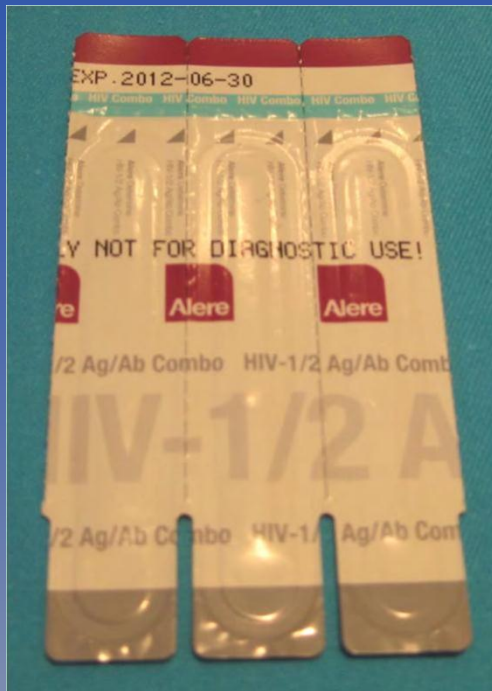
Detects HIV 1 p24 Antigen HIV 1/2 IgG and IgM Antibodies

- Bio-Rad GS HIV Combo Ag/Ab EIA
- Abbott Architect Ag/AB Combo
Time to results ~ 29 minutes



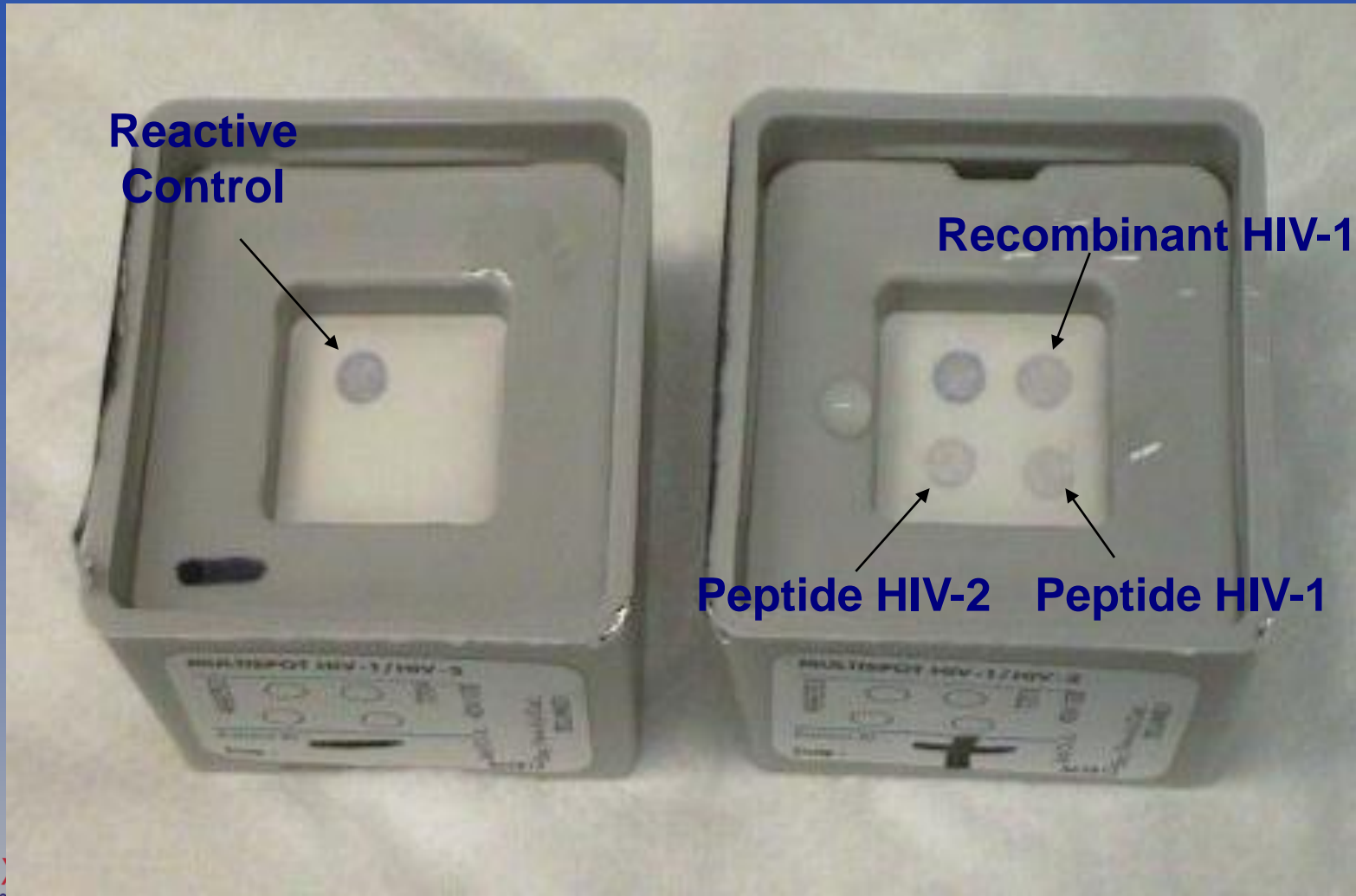
Determine Combo Rapid HIV 1/2 Ag-Ab Test

Alere – 4th generation technology
Moderately Complex – NOT CLIA Waived

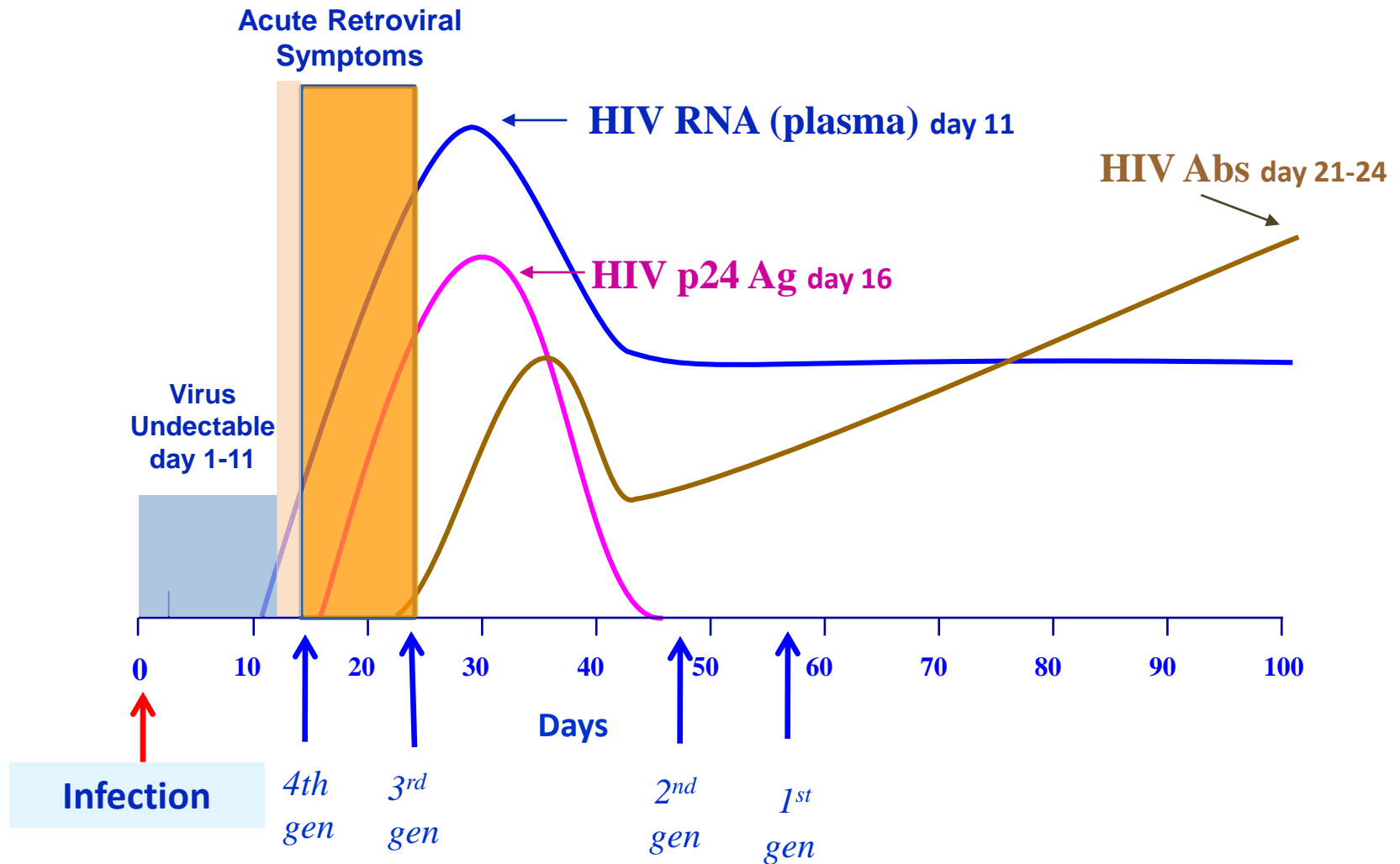


MultiSpot

FDA-approved HIV-1/HIV-2 Antibody Differentiation Assay



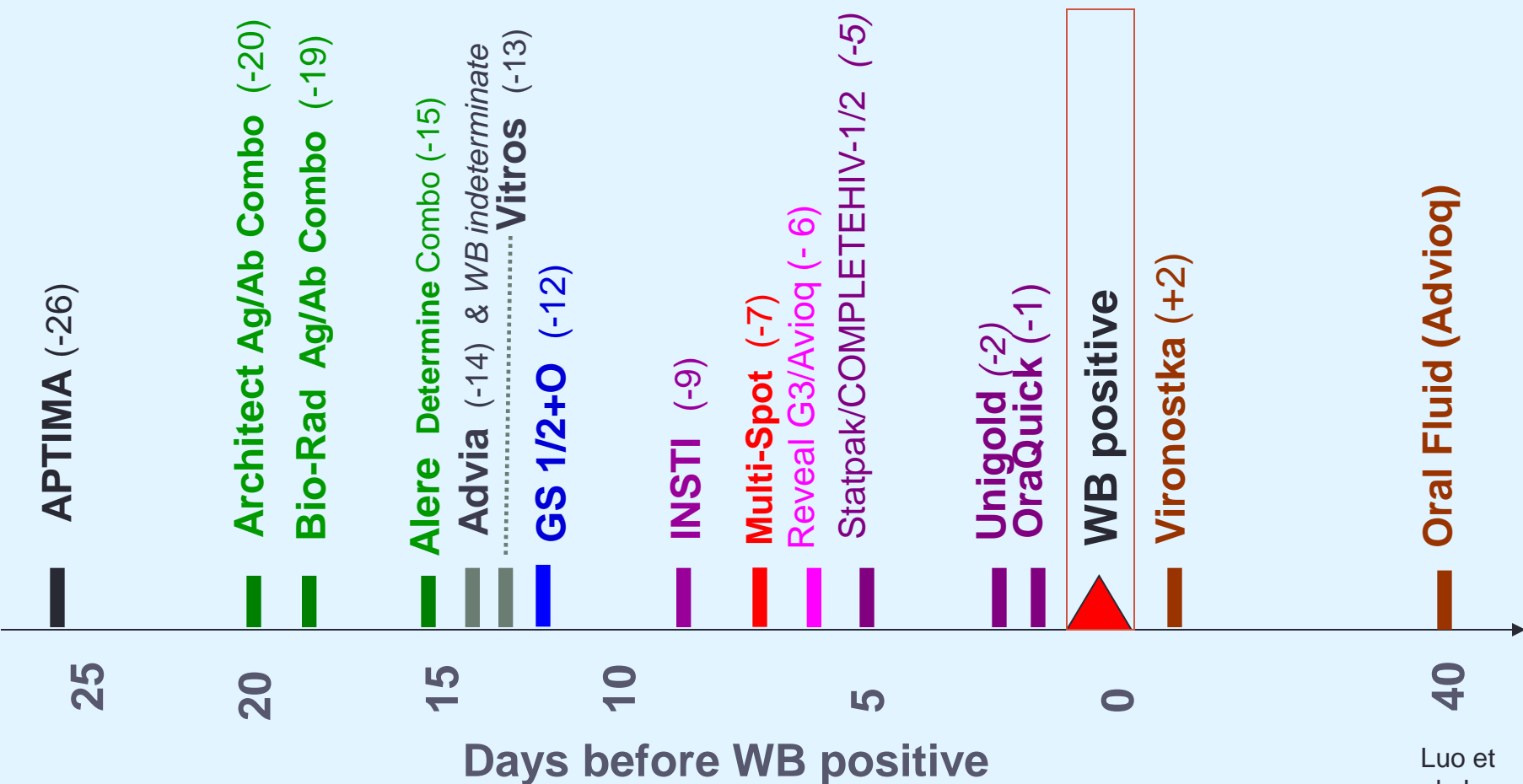
HIV Infection and Laboratory Markers



Modified after Busch et al. Am J Med. 1997

Sequence of Test Positivity Relative to WB (plasma)

166 specimens, 17 Seroconverters - 50 % Positive Cumulative Frequency



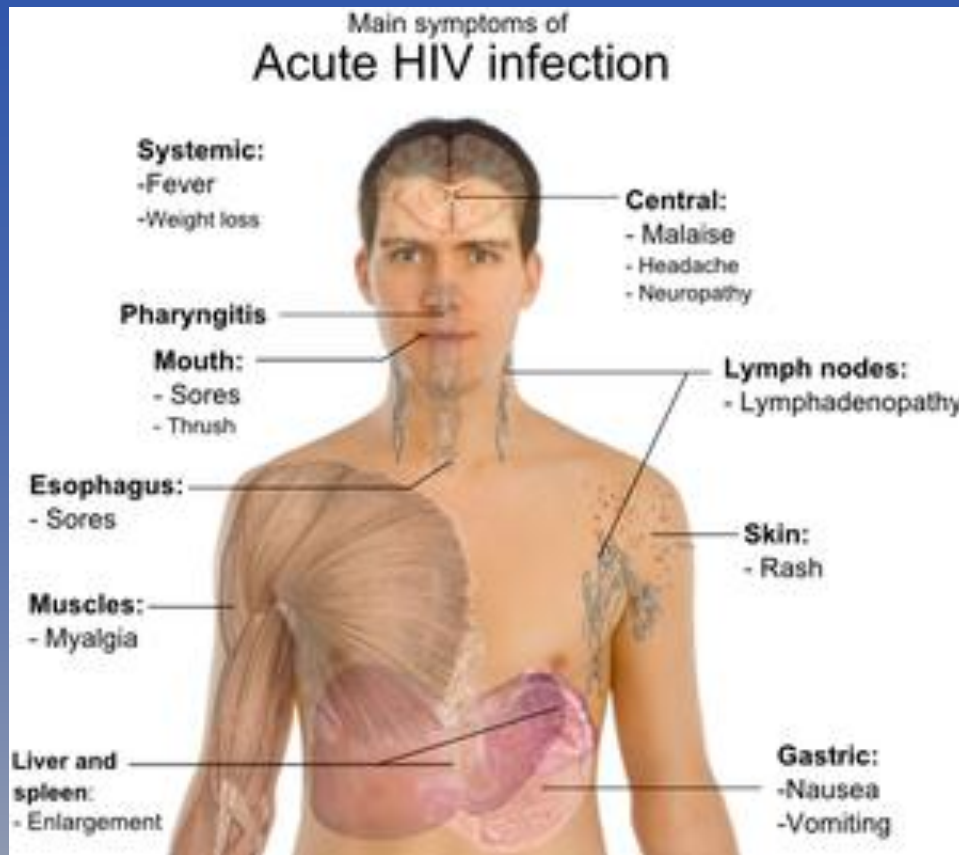
Modified from Masciotra et al, J Clin Virol 2011 and Owen et al, J Clin Micro 2008

Luo et al, J Clin Virol 2013

Limitations of the 1989 Algorithm

- Western blot is less sensitive during early infection than most screening tests in current use,
- Antigen/antibody combo tests can detect most antibody-negative persons during highly infectious acute infection stage,
- Because of cross-reactivity more than 60% of persons with HIV-2 infection are misclassified as HIV-1 by Western blot

Acute Viral Infection



- Malaise/fatigue
- Fever/chills/night sweats
- Weight loss, loss of appetite
- Sore throat
- Nausea/vomiting/diarrhea
- Swollen lymph nodes
- Aching muscles or joints
- Rash
- Rarely headache, neurologic symptoms

Clinical Syndrome of Acute HIV

40% – 90% develop symptoms of Acute HIV

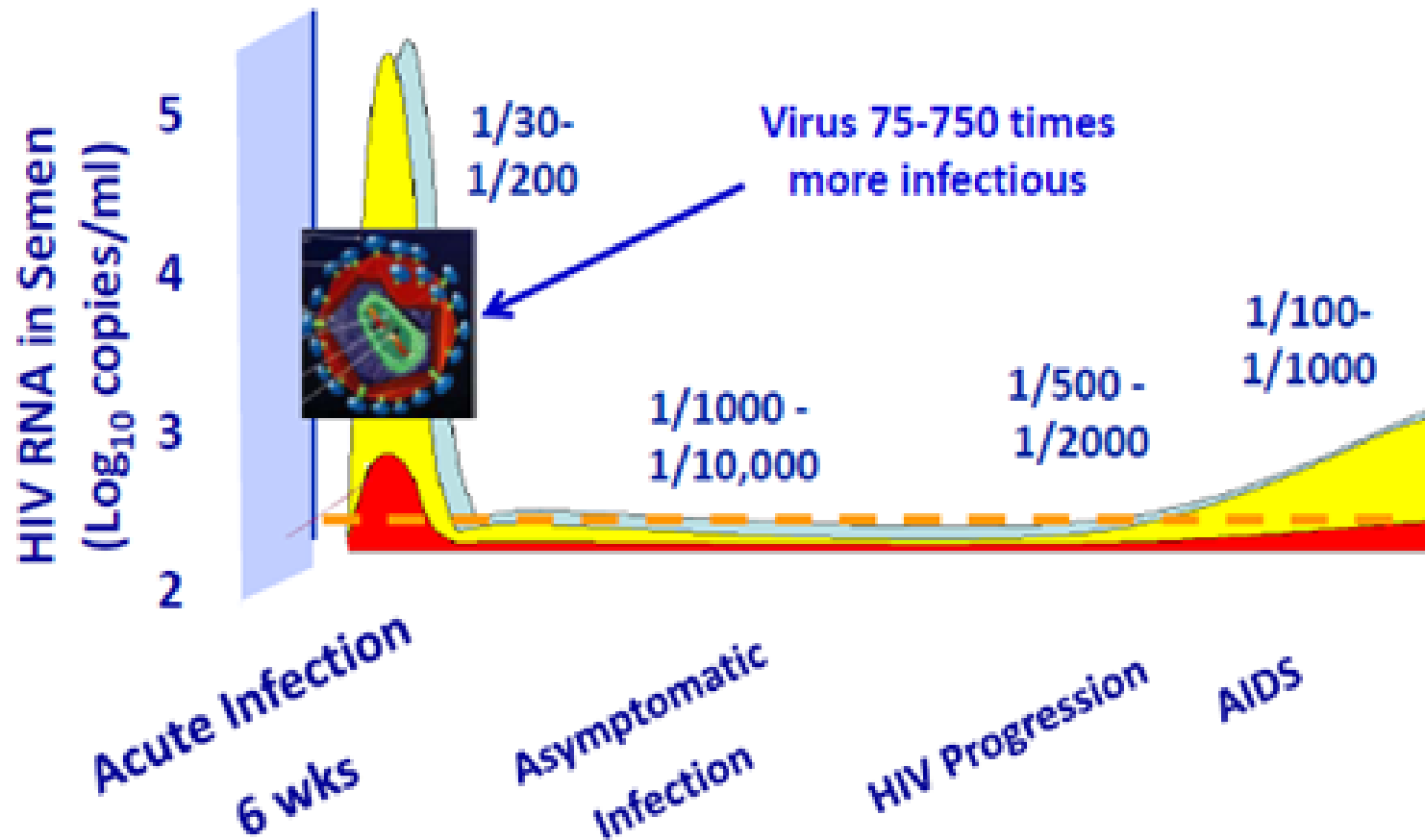
→ 50% – 90% w/ symptoms seek medical care

Of those diagnosed with Acute HIV

→ 50% of patients were seen at least 3 times before diagnosis

Kahn et al, NEJM 1998, Weintrob et al, Arch Int Med 2003

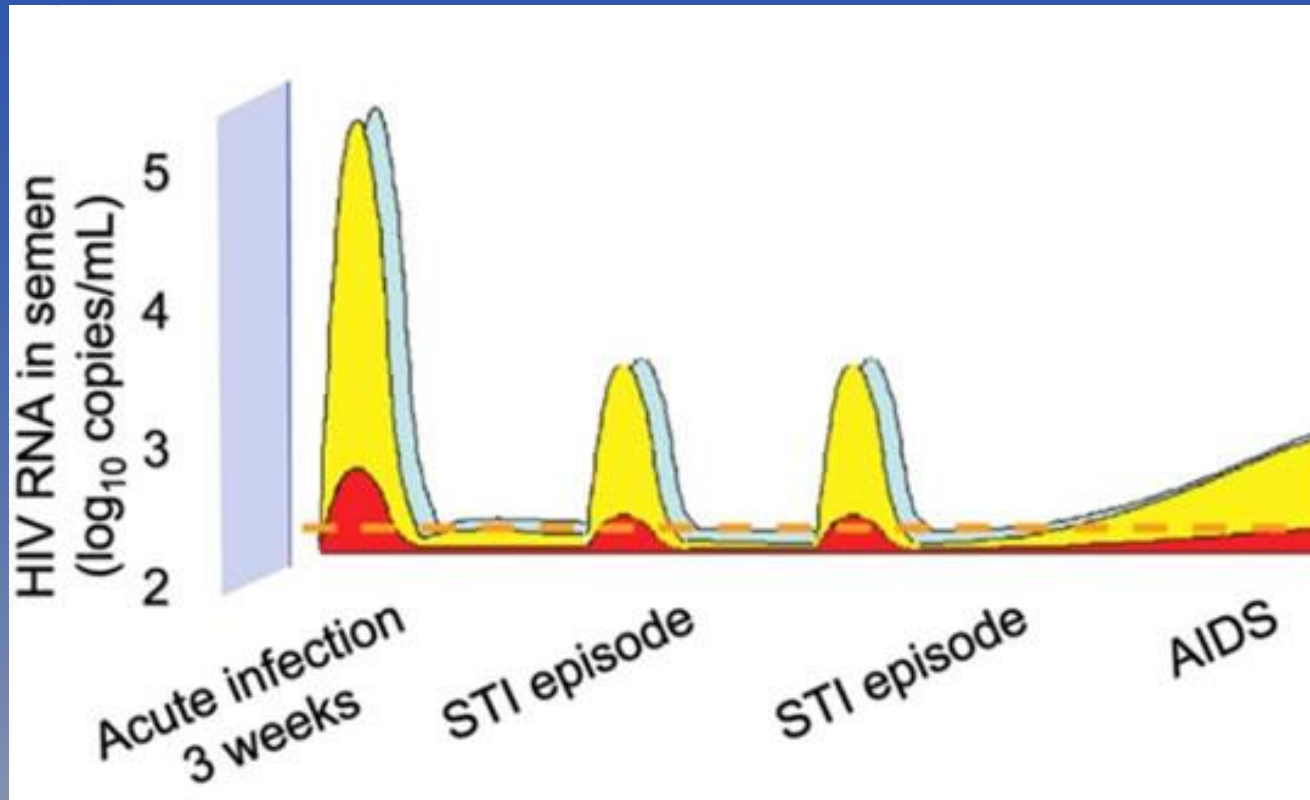
Acute Infection: Increased Risk of Sexual Transmission of HIV



Ma, J Virol 2009

Cohen & Pilcher, J Infect Dis. 2005

Prediction of the efficiency of HIV transmission according to HIV burden in the genital tract.

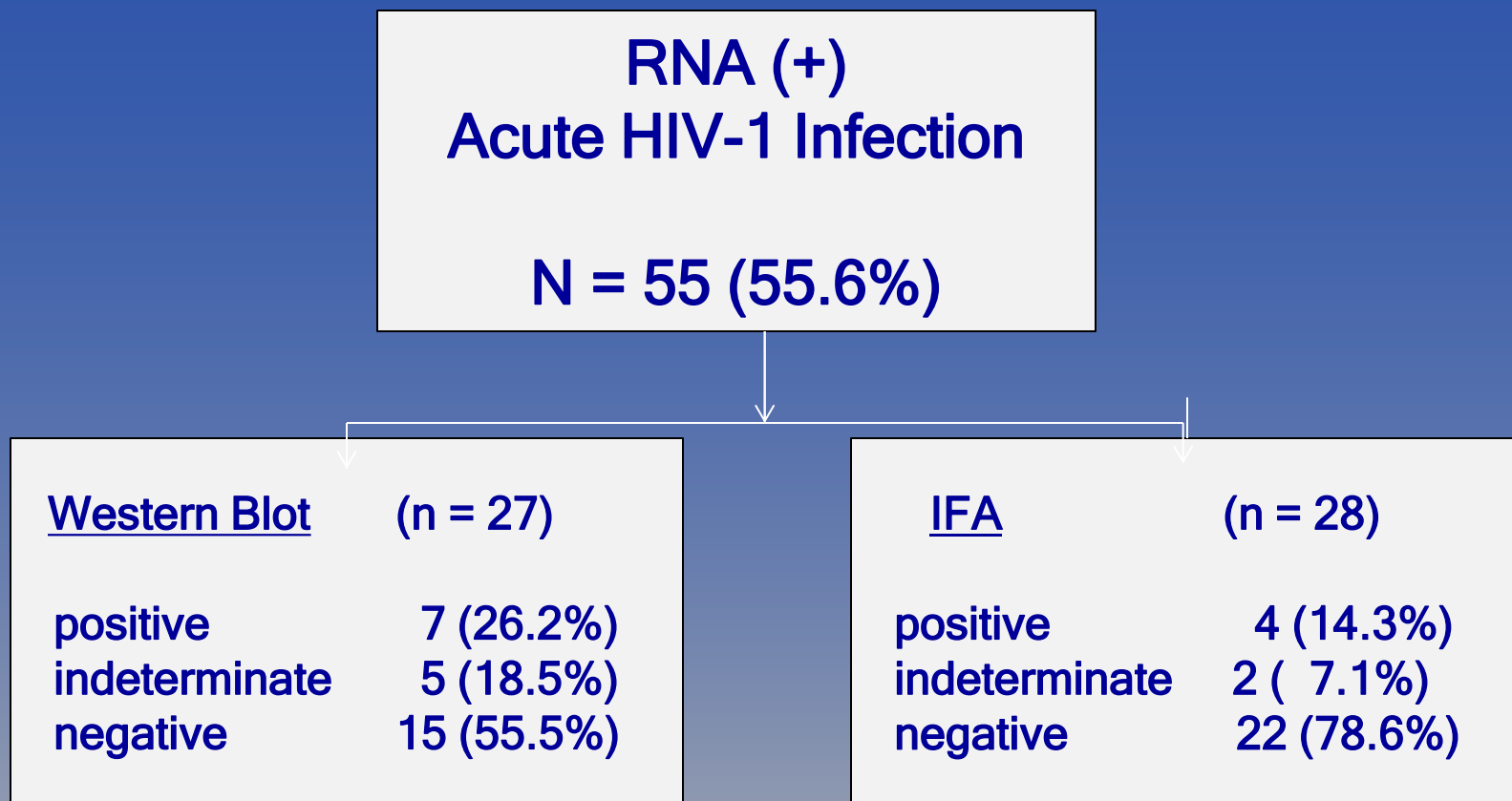


Cohen M S , and Pilcher C D J Infect Dis. 2005;191:1391-1393
© 2005 by the Infectious Diseases Society of America

4th Generation HIV-1/2 immunoassay Test Results

New York City, San Francisco, North Carolina

2011-2012



Routine Medical Setting NAAT Submissions and Results 2012-July 2014

Submitter	# Samples	AHI	Positivity Rate
Medical System 1	114	9	7.89
Medical System 2	124	9	7.26
Hospital 3	23	1	4.35
Hospital 4	16	4	25.00
Hospital 5	3	1	33.33
Hospital 6	10	0	0.00
Medical System 7	23	3	13.04
Hospital 8	1	0	0.00
Medical System 9	3	0	0.00
TOTAL	317	27	8.52

HIV Testing Recommendations from CDC/APHL



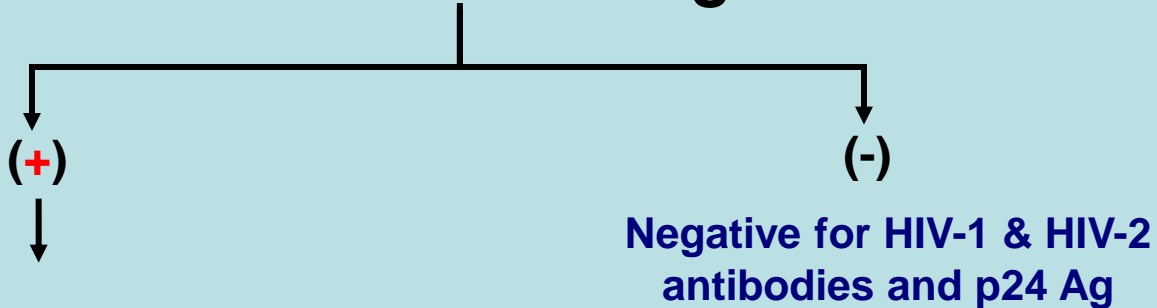
Transitions and Change Benefits and Challenges

Please Ponder.....

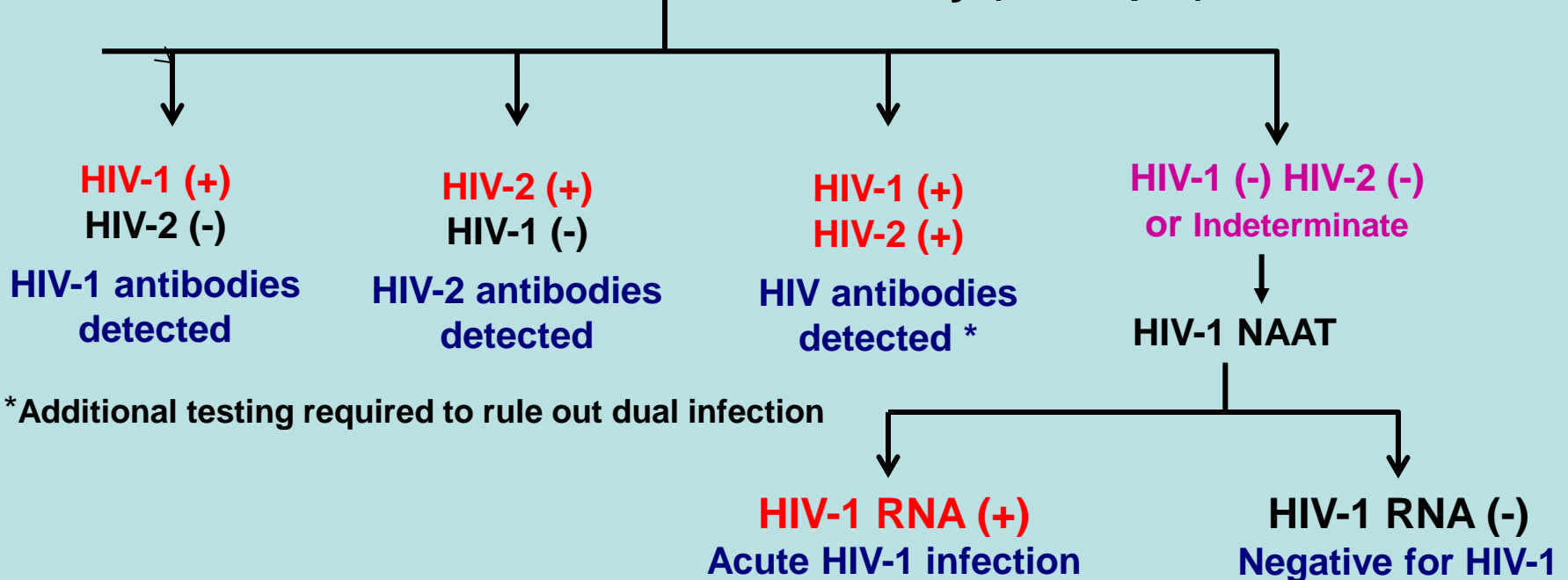
How can this improve your services,
the quality of care your patients receive
and the overall health of your
community?

New HIV Testing Algorithm

4th generation HIV-1/2 Combo Ag/Ab Immunoassay



HIV-1/HIV-2 differentiation immunoassay (MultiSpot)



* Additional testing required to rule out dual infection

New HIV Testing Algorithm Results

Lab Report Language	Interpretation for Patients
Negative. HIV-1 p24 antigen, HIV-1 and HIV-2 antibodies not detected.	If client did not have risk in 16 days before the test or since, client does not have HIV.
Positive. HIV-1 antibodies detected.	The client has HIV-1.
Positive. HIV-2 antibodies detected.	The client has HIV-2.
Positive. A reactive HIV antigen/antibody test and a positive HIV-1 RNA test indicate acute HIV-1 infection.	The client has HIV-1 and the test result indicates that s/he was recently infected (likely infected 2-8 weeks before taking the test).
Negative. HIV antibodies not detected. No detectable HIV-1 RNA. HIV-2 infection cannot be excluded if recent exposure is suspected.	The client does not have HIV-1. The client should be retested in two weeks to rule out possibility of acute HIV-2.

TABLE 1.

OQ RT-FS- OraQuick Fingerstick, OQ RT-OF- OraQuick Oral Fluid, I- Indeterminate, OQ- OraQuick, UG-UniGold, SR-StatPak, MS-MultiSpot, NR- nonreactive, N-neg, R-Reactive, R1- Reactive HIV1.

Summary of assay performance results with specimens from acutely infected and recently infected individuals^a

Sample ID	Initial screen	First-gen or second-gen EIA		WB	Third-gen EIA					MS	Viral load (copies/ml) ^b	Fourth-gen IA	
		Avg S/C	Result		Avg S/C	Result	RT	RT	RT	Avg S/CO		Result	
A	First-gen EIA	0.351	NR	I	0.127	NR	N	N	N	N	5,770 [†]	0.37	NR
B	First-gen EIA	0.602	NR	I	0.955	NR	N	N	N	N	≥500,000 [†]	611.12	R
C	First-gen EIA	0.440	NR	I	≥14.658	R	N	R	N	N	12,183 [†]	1.62	R
E	First-gen EIA	0.368	NR	I	0.233	NR	N	N	N	N	6,373 [†]	0.65	NR
F	First-gen EIA	0.329	NR	I	13.433	R	N	R	N	R1	≥500,000 [†]	85.73	R
G	First-gen EIA	0.317	NR	N	0.084	NR	N	N	N	N	12,852 [†]	0.74	NR
H	First-gen EIA	0.338	NR	I	0.109	NR	N	N	N	N	14,062 [†]	0.68	NR
I	First-gen EIA	0.646	NR	I	≥14.658	R	R	R	R	R1	≥500,000 [†]	67.70	R
J	First-gen EIA	0.358	NR	N	0.106	NR	N	N	N	N	3,921 [†]	0.23	NR
K	First-gen EIA	0.346	NR	N	4.574	R	N	R	N	N	≥500,000 [†]	43.92	R
L	First-gen EIA	0.373	NR	N	0.175	NR	N	R	N	N	≥500,000 [†]	39.55	R
M	OQ RT-FS	0.344	NR	N	1.5327	R	N	N	N	N	≥500,000 [†]	368.21	R
N	First-gen EIA	0.337	NR	N	0.113	NR	N	N	N	N	1,177 [†]	0.21	NR
O	OQ RT-FS	0.301	NR	N	0.127	NR	N	N	N	N	≥500,000 [†]	61.32	R
P	First-gen EIA	0.755	NR	N	≥14.658	R	N	R	N	R1	≥500,000 [†]	136.62	R
Q	First-gen EIA	0.311	NR	N	0.277	NR	N	N	N	N	43,173 [†]	1.80	R
R	OQ RT-FS	0.642	NR	I	0.117	NR	N	N	N	N	30,734 [†]	2.05	R
S	First-gen EIA	0.406	NR	N	13.276	R	N	R	N	R1	≥500,000 [†]	219.97	R
T	OQ RT-OF	0.401	NR	N	4.929	R	N	N	N	N	≥500,000 [†]	268.30	R
U	OQ RT-FS	0.325	NR	N	0.195	NR	N	N	N	N	≥500,000 [†]	317.71	R

Acute HIV: Partner Notification

- Persons with acute HIV infection named
 - 2.5 times as many sex partners
 - 1.9 times as many partners newly diagnosed with HIV
 - ...as did persons with new diagnosis of established HIV infection

-Moore et al, JAIDS 2009

Discordant Results

- 2012 DSHS lab 30% Indeterminate and Negative Oral Fluid WBs.
- RNA Testing
 - Resolves HIV 1 infections
- Dallas and Houston Health Departments

Case Studies

- 18 yo male rapid test INSTI prelim +
 - Oral fluid OraSure confirmatory WB negative
 - No blood specimen to NAAT test
- 26 yo male screening 4th gen +
 - MultiSpot negative
 - NAAT +, VL 160K copies.
- 30 yo pregnant woman
 - 3rd gen +
 - WB Indeterminate
 - NAAT +

DSHS HIV/STD Policy 2013.02

- *The Use of Testing Technology to Detect HIV Infection*
 - Blood-based specimens (finger stick or venipuncture).
 - Confirmatory testing collected by venipuncture on-site immediately after a point of care (e.g., rapid) preliminary positive test result.
 - All indeterminate and non-reactive confirmatory tests must be automatically referred for a NAAT to determine if a client has an acute HIV Infection.

Transition to Best Practices

- Current Test Technology Used
- Staff training
 - Technology
 - Specimen Collection
 - Messaging/Counseling
- Administration
- Link to Care
- Public Health Follow up

Specimen Collection

- 4th Gen HIV 1, 2 Antigen/Antibody
 - No more than 5 days cold.
 - Gold top, tiger top, spin before submit. NO DRY BLOOD SPOT.
 - Reactive samples run in duplicate.
- MultiSpot HIV 1/2 Differentiation
 - Reflex from reactive 4th Gen.
 - 25 minute average run time. Read immediately once test completed.

Specimen Submission to DSHS Lab

- For initial testing or if a rapid HIV test was preliminary positive, check **HIV Combo Ag/Ab EIA** (serum).
 - If positive, it will reflex to the Multispot for confirmation.
- Discordant results (e.g., 4th Gen is reactive and the Multispot is non-reactive), DSHS Austin Lab will submit the specimen to the Dallas County HHS Laboratory for NAAT to determine acute HIV infection.

Overview

- 10% of infections are Ab neg and have AI.
- 4th Gen will identify 89%
- First 8 weeks of infection account for 15 - 50% of transmissions.
- 10 - 20% more infectious and engage in high risk behaviors.

DSHS Laboratory Reporting Language

HIV Reporting:

HIV Combo Ag/Ab EIA

Nonreactive

Note:

- * HIV Combo Ag/Ab EIA Reference Range = Nonreactive
- * The HIV testing is not, in and of itself, diagnostic for HIV infection and should be considered in conjunction with other laboratory test results, clinical presentation and patient history. Only a physician should interpret the results.
- * HIV screening performed by the 4th generation HIV Combo Ag/Ab EIA test for HIV detection do not distinguish between the presence of HIV antibodies or antigen in a sample. Additional supplemental tests will be automatically performed to verify the presence of HIV-1 p24 antigen or antibodies to HIV-1 or HIV-2.
- * A person who has antibodies to HIV-1 is presumed to be infected with the virus, except a person who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV.

HIV Reporting:

HIV Combo Ag/Ab EIA

Reactive

Note:

HIV Combo Ag/Ab EIA Reference Range = Nonreactive

The HIV testing is not, in and of itself, diagnostic for HIV infection and should be considered in conjunction with other laboratory test results, clinical presentation and patient history. Only a physician should interpret the results.

HIV screening performed by the 4th generation HIV Combo Ag/Ab EIA test for HIV detection do not distinguish between the presence of HIV antibodies or antigen in a sample. Additional supplemental tests will be automatically performed to verify the presence of HIV-1 p24 antigen or antibodies to HIV-1 or HIV-2.

A person who has antibodies to HIV-1 is presumed to be infected with the virus, except a person who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV.

Multispot HIV-1/HIV-2 Rapid EIA

HIV-1 Reactive

Note:

Multispot Reference Range = Nonreactive

The Multispot HIV-1/HIV-2 Rapid Test (MS) cannot be used as part of a diagnostic testing algorithm for both the initial testing and the differentiation of the same sample.

If MS result is undifferentiated and cannot be differentiated between HIV-1 and HIV-2, follow up with additional testing to rule out dual infection with HIV-1 and HIV-2.

If MS result is indeterminate for HIV-1, follow up with NAAT to rule out acute HIV-1 infection.

A nonreactive MS result for an individual subject indicates absence of detectable HIV antibodies. However, a nonreactive test result does not preclude the possibility of exposure to or infection with HIV 1 and/or HIV 2.

If MS result is invalid, submit a fresh sample to rule out HIV infection.

HIV Reporting:

HIV Combo Ag/Ab EIA

Reactive

Note:

HIV Combo Ag/Ab EIA Reference Range = Nonreactive

The HIV testing is not, in and of itself, diagnostic for HIV infection and should be considered in conjunction with other laboratory test results, clinical presentation and patient history. Only a physician should interpret the results.

HIV screening performed by the 4th generation HIV Combo Ag/Ab EIA test for HIV detection do not distinguish between the presence of HIV antibodies or antigen in a sample. Additional supplemental tests will be automatically performed to verify the presence of HIV-1 p24 antigen or antibodies to HIV-1 or HIV-2.

A person who has antibodies to HIV-1 is presumed to be infected with the virus, except a person who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV.

Multispot HIV-1/HIV-2 Rapid EIA

Nonreactive

Note:

Multispot Reference Range = Nonreactive

The Multispot HIV-1/HIV-2 Rapid Test (MS) cannot be used as part of a diagnostic testing algorithm for both the initial testing and the differentiation of the same sample.

If MS result is undifferentiated and cannot be differentiated between HIV-1 and HIV-2, follow up with additional testing to rule out dual infection with HIV-1 and HIV-2.

If MS result is indeterminate for HIV-1, follow up with NAAT to rule out acute HIV-1 infection.

A nonreactive MS result for an individual subject indicates absence of detectable HIV antibodies. However, a nonreactive test result does not preclude the possibility of exposure to or infection with HIV 1 and/or HIV 2.

If MS result is invalid, submit a fresh sample to rule out HIV infection.

HIV-1 Nucleic Acid Amplification Test (NAAT)

Reactive

Note:

Nucleic Acid Amplification Test is performed by the Dallas Co. Dept. Of Health and Human Services at: 2377 N. Stemmons Freeway, Dallas TX 75207, CLIA # 45D0672012.

A copy of the Dallas report is attached if the NAAT is performed.

If NAAT reactive, possible acute HIV infection. Refer to physician for care.

If NAAT nonreactive submit second sample to rule out HIV infection if clinically suspected.

If Multispot / WB reactive, Nucleic Acid Amplification Test (NAAT) is not indicated per CLSI guidelines. Submitter notified.

If "Quantity Not Sufficient" for NAAT, submit second sample to rule out acute HIV infection.

HIV Reporting:

Multispot HIV-1/HIV-2 Rapid EIA	HIV-1 Reactive
	HIV-2 Reactive
	HIV Reactive (Undifferentiated)
	Indeterminate
	Nonreactive for HIV-1 and HIV-2
	Invalid

Note:

Multispot Reference Range = Nonreactive

The Multispot HIV-1/HIV-2 Rapid Test (MS) cannot be used as part of a diagnostic testing algorithm for both the initial testing and the differentiation of the same sample.

If MS result is undifferentiated and cannot be differentiated between HIV-1 and HIV-2, follow up with additional testing to rule out dual infection with HIV-1 and HIV-2.

If MS result is indeterminate for HIV-1, follow up with NAAT to rule out acute HIV-1 infection.

A nonreactive MS result for an individual subject indicates absence of detectable HIV antibodies. However, a nonreactive test result does not preclude the possibility of exposure to or infection with HIV 1 and/or HIV 2.

If MS result is invalid, submit a fresh sample to rule out HIV infection.

Laboratory Testing for the Diagnosis of HIV Infection Updated Recommendations

<http://www.cdc.gov/hiv/pdf/HIVtestingAlgorithmRecommendation-Final.pdf>

CDC Home



Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People.™

☒ HIV/AIDS Prevention only

☐ All CDC Topics

Choose a topic above

SEARCH

A-Z Index for All CDC Topics

HIV/AIDS

HIV/AIDS

HIV Basics

Who's at Risk for HIV?

HIV Testing

Background

US HIV Tests

► Laboratory Tests

CLIA-Waived Tests

Home Testing

Testing in Non-Clinical
Settings

Testing in Clinical
Settings

Living With HIV

Prevention Research

Policies and Programs

Guidelines and
Recommendations

Training and Conferences

Statistics Center

Resource Library

[HIV/AIDS](#) > [HIV Testing](#) > [US HIV Tests](#)

Recommend

Tweet



Share

Laboratory Tests

In this section we provide resources for all FDA-approved diagnostic HIV tests for use in moderate and high complexity laboratories

Laboratory Testing Guidance

- **NEW!** Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations
- **NEW!** Quick Reference: Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens
- APHL Suggested Reporting Language for the HIV Laboratory Diagnostic Testing Algorithm

FDA Approved HIV Tests

- **NEW!** Advantages and Disadvantages of Different Types of HIV tests
- **NEW!** List of Moderate Complexity Rapid HIV Tests for Laboratory Use
- **NEW!** List of Moderate and High Complexity HIV tests for Laboratory Use



HIV A-Z Topics

Print page

Get email updates

Subscribe to RSS

See RSS

Listen to audio/Podcast

VIH En Español (Spanish)

Find an HIV Testing Site

City, State/ZIP

5 miles

GO

Find an HIV testing site near you.

For additional HIV services, select the "More" tab.

Resources

To order materials from the DSHS Warehouse:

<http://www.dshs.state.tx.us/hivstd/info/edmat.shtm>

- www.aphl.org/aphlprograms/infectious/hiv/Pages/HIV-Diagnostic-Testing-Algorithm.aspx
- www.hivtestingconference.org
- www.hivforum.org/index.php?option=com_content&task=view&id=774&Itemid=92
- http://jid.oxfordjournals.org/content/202/Supplement_2/S270.full.pdf+html

Acknowledgements

- Bernard Branson, MD - CDC
- Michelle Owen, Ph.D- CDC
- Joanne Steckler, MD - UW
- Isabel Clark, MS - DSHS
- Nicole Messenger, MPH - DSHS
- Peter Leone, MD - UNC
- Barry Callis, Massachusetts
- Tammy Goodhue, Massachusetts

Jenny McFarlane
Manager, HIV Testing and Prevention
Interventions Team
DSHS HIV/STD/TB Viral Hepatitis Unit